REMARKS

Status of claims:

Claims 1, 5-8, 10, 13-15, 17-34, 36-45 and 48-66 were pending. Claims 5-8 and 51-62 were withdrawn as drawn to non-elected subject matter. Claims 1, 10, 13-15, 17-34, 36-45, 48-50 and 63-66 were under examination. Claim 10 is canceled and the limitations of Claim 10 are incorporated into Claim 1. Claims 1, 18, 24-25, 32, 37, 44, 45, 63-66 are currently amended. Claims 67-73 have been added. Applicant submits that no new matter is added by the amendment.

Amendment to the Specification

The Specification has been amended to include essential matter, which was present in the applications that were incorporated by reference in the instant application. Accordingly, a sequence listing is also submitted.

Support for Paragraph [0130] can be found on pages 4-5 of Application Serial No. 60/399,707, which was incorporated by reference in the instant application at Paragraphs [0060] and [0066]. Support for Paragraph [0131] can be found on page 16 of Application Serial No. 60/360,229, which was incorporated by reference in the instant application at paragraph [0059] and [0066]. Support for Paragraph [0132] can be found on page 18-19 of Application Serial No. 60/360,259, which was incorporated by reference in the instant application at paragraph [0062]. Support for Paragraph [0133] can be found on page 5 of Application Serial No. 60/388,314, which was incorporated by reference in the instant application at paragraphs [0058] and [0066]. Support for Paragraph [0134] can be found in paragraph [0022] of the published Application Serial No. 10/116,116, which was incorporated by reference in the instant application at paragraphs [0058] and [0066].

Amendment to the Claims

Examiner had objected to claims 10, 18, 20, 32, 37, 39 and 45 for being dependent from a rejected independent claim. Applicants have amended Claim 1 to include the elements previously recited in Claim 10 and canceled Claim 10. Applicants have amended Claims 18, 32, 37 and 45 so that they are in independent form and no longer depend from a rejected independent claim.

Since Claims 20 and 39 depend from amended Claims 18 and 39, they also are no longer dependent on a rejected independent claim.

Claims 25, 26, 44 and 45 are amended to delete the antibody MN-14 from the claimed subject matter.

Claims 63-66 are amended to include the antibodies MN-14, hLL1, hRS7, hPAM04 and hMu-9. Support for MN14 can be found at least at paragraph [0053] of the published application, as well as in original claims 25, 26, 44, 45, 46, 47, 61 and 62. Support for hLL1 can be found at least at paragraph [0065] of the published application. Support for hRS7 can be found in application Ser. No. 60/360,229 (publication number US2004/0001825A1) which was incorporated by reference in the instant application at paragraph [0066]. Support for hPAM04 can be found in application Ser. No. 60/388,314 (publication number US2005/0014207A1)which was incorporated by reference in the instant application at paragraph [0066]. Support for hMu-9 can be found in application Ser. No. 10/116,116 (publication number US2005/0169926A1) which was incorporated by reference in the instant application at paragraph [0066].

Claims 67-73 are new and include the CDR sequences of the antibodies RS7 and hRS7, LL1 and hLL1, hA20, PAM-4 and hPAM4, Mu-9 and hMu-9, anti-AFP-31 and humanized anti-AFP31 and MN-14 respectively. Support for the Claim 67 can be found in the newly inserted Paragraph [0131] and in Figures 2A, 2B, 4A and 4B of application Ser. No. 60/360,229, which was incorporated in its entirety in the instant application at Paragraphs [0058] and [0066]. Support for Claim 68 can be found can be found in the newly inserted Paragraph [0132] and at Figures 1A, 1B, 4A and 4B of application 60/360,259, which was incorporated in its entirety in the instant application at Paragraph [0062]. Support for Claim 69 can be found in Figures 1A, 1B, 5A, 5B and 5C of the Application Ser. No. 60/416,232, which was published prior to the effective filing date of the instant application. Support for Claim 70 can be found in newly inserted Paragraph [0133] and Figures 1A, 1B, 4A and 4B of the application Ser. No. 60/388,314, which was incorporated in its entirety in the instant application at Paragraphs [00058] and [0066]. Support for Claim 71 can be found in the newly inserted Paragraph [0134] and in Figures 1A, 1B, 4A and 4B of the application Ser. No. 10/116,116, which was incorporated in its entirety in the instant application at Paragraphs [0058] and [0066]. Support for Claim 72 can be found in the newly inserted Paragraph [0130] and in Figures 1A, 1B, 5A and 5B of the application Ser. No.

60/399,707, which was incorporated in its entirety in the instant application at Paragraphs [0060] and [0066]. Support for Claim 73 can be found in Figures 7 and 8 of the U.S. Patent No. 5,874,540, which was published prior to the effective filing date of the instant application.

Claim Rejections - 35 USC § 112, first paragraph

Claims 25, 26, and 44– antibodies LL2, CC49, J591, L243

The Action rejected claims 25-26 and 44 for failure to comply with the enablement requirement, because "the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description." [Action at pg. 2] The Action further states that, "As required elements [the antibodies] must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public." [Action at pg. 2-3]

While Applicant traverses the requirement for a deposit, in the interests of advancing prosecution, Applicant points out that antibody LL2 was deposited with the American Tissue Culture Collection (ATCC) under the accession number ATCC PTA-6735; the hybridoma cell line for the antibody G250 was deposited at the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) under accession number 2526, for antibody CC49 was deposited with the ATCC under accession number ATCC HB 9459, for antibody J591 was deposited with the ATCC under accession number HB 12126, and for antibody L243 was deposited with the ATCC under accession number ATCC HB 55. Thus, Applicant states that all antibodies recited in amended claims 24-25 and 44 were deposited under the terms of the Budapest Treaty and that as required by 37 C.F.R. 1.808, access to the deposits will be available during pendency of the patent application and all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent. Therefore, the applicant respectfully submits that the rejection over failure to deposit these antibodies be withdrawn.

Claims 63-66 – antibodies RS7, LL1, hA20, PAM-4, Mu-9, AFP-31, MN-14, hRS7, hLL1, hPAM4 and hMu9

The Action rejected claims 63-66 for failure to comply with the enablement requirement and required deposit of these antibodies. Applicant respectfully submits that deposit is not required in this case to satisfy the enablement requirement, as these antibodies were reported prior to the effective filing date of the instant application.

RS7 and hRS7 antibodies: Provisional application 60/360,229 filed 3/1/2002 and incorporated by reference in the instant application discloses the RS7 and hRS7 antibodies. Specifically Figures 2A and 2B disclose the complete nucleotide and amino acid sequences of the RS7 variable light and heavy chains and Figures 4A and 4B disclose the nucleotide and amino acid sequences of the humanized RS7 variable light and heavy chains, including the CDR sequences of these chains.

The Action appears to assert that although the CDR and variable domain sequences were disclosed in the application, further disclosure of human or other constant region sequences was required for enablement purposes. However, it is well established in patent law that what is well known in the art need not be disclosed to satisfy the requirements of 35 U.S.C. § 112, first paragraph. According to MPEP § 2164.08,

> Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The Applicant respectfully submits that the constant region sequences of a wide variety of human and other antibodies, as well as methods of making humanized antibodies from known variable domain sequences were well known in the art as of the instant priority date, and were not required for enablement of the instant claimed antibodies comprising the disclosed variable domains and/or CDR sequences of the RS7 and hRS7 antibodies.

Additionally, the application at pages 11-16 also discloses details of how to prepare the antibodies. It further provides details of how to prepare antibody fragments and antibody fusion proteins on pages 17-22 and how to use these antibodies in treatment and diagnosis of diseases on pages 24-44. Furthermore, Example 2 (on page 45) explicitly teaches the skilled artisan how to

construct the hRS7 antibody, including providing details on design and synthesis of the variable region sequences, primers used in the PCR amplification, cloning of the PCR amplified products into the expression vector hRS7pdHL2, conditions for transfection and expression of the hRS7 antibody and determination of the binding activity of the antibody. The pdHL2 vector, containing immunoglobulin constant domains, was also publicly known as of the instant priority date. For example, U.S. Patent No. 5,650,150 (Gillies et al., issued 1997) starting at Col. 7, line 7, under "Plasmid Construction" states that, "Described below is the construction of PdHL2, a plasmid which contains the human Cγ1 heavy and kappa light chain gene sequences as well as insertion sites for V region cDNA cassettes (Gillies et al. (1989) J. Immunol. Meth. 125:191). This plasmid may be used as a starter plasmid for constructing any IgH chain cytokine fusion."

Thus, once the variable region and CDR sequences for the RS7 and hRS7 antibodies were disclosed in the instant application, it would have been a matter of routine experimentation for the skilled artisan to make and used the claimed antibodies following the detailed methodology disclosed in Example 2 of the incorporated application. Expression vectors containing human constant region sequences, into which the variable region sequences could be easily inserted by standard techniques, were known in the art, as exemplified by the pDHL2 vector described in U.S. Patent No. 5,650,150.

Applicant therefore submits that the claimed subject matter involving RS7 and hRS7 antibodies is fully enabled by the instant Specification, in light of general knowledge in the art, and that no deposit should be required for these antibodies, since the complete CDR and variable region sequences of the antibodies are fully known.

Similarly, the claimed subject matter involving the other antibodies is also fully enabled.

LL1 and hLL1: Provisional application 60/360,259 filed 3/1/2002, incorporated by reference, discloses the LL1 and hLL1 antibodies. [See in the Published Application Fig. 1A, 1B, 4A and 4B for the complete nucleotide and amino acid sequences of the variable light and heavy chains of the antibodies; pages 12-16 for discussion of preparation of monoclonal antibodies, pages 16-18 for production of antibody fragments, pages 40-42 for expression vectors used, pages 42-44 for methods of making the antibodies, and Examples 6-7 for the PCR amplification, cloning and transfection protocols for preparing h-LL1 antibody.].

hA20: Provisional application 60/416,232 filed 10/7/02 discloses the hA20 antibody. [See in the Published Application Fig. 1A, 1B, 5A, 5B and 5C for the complete nucleotide and amino acid sequences of the variable light and heavy chains of the antibodies; pages 23-27 for discussion of preparation of monoclonal antibodies, pages 27-28 for production of antibody fragments, pages 45-46 for expression vectors used, pages 46-52 for methods of making antibodies and Examples 1-3 for the PCR amplification, cloning and transfection protocols for preparing the hA20 antibody.] Although this application was not incorporated by reference in the instant application, it was published and, therefore, the antibody was publicly known at the effective filing date of the instant application.

Mu-9 and hMu-9: Provisional application 10/116,116 filed 4/5/02, incorporated by reference, discloses the details of Mu-9 and hMu-9 antibodies. [See the Published Application Fig. 1A, 1B, 4A and 4B for the complete nucleotide and amino acid sequences of the variable light and heavy chains of the antibodies; pages 28-41 for discussion of preparation of monoclonal antibodies, pages 41-48 for production of antibody fragments, and Examples 10-12 for PCR amplification, cloning and transfection protocols for preparing hMu-9 antibody.].

PAM-4 and hPAM-4: Provisional application 60/388,314 filed 6/14/02, incorporated by reference, discloses the PAM-4 and hPAM-4 antibodies. [See in the Published Application Fig. 1A, 1B, 4A and 4B for the complete nucleotide and amino acid sequences of the variable light and heavy chains of the antibodies; pages 24-27 for preparation of antibodies, pages 27-28 for production of antibody fragments, and Example 7 for the PCR amplification, cloning and transfection protocols for preparing h-PAM4 antibody.]

AFP-31 and hAFP31: Provisional application 60/339,707, filed 8/1/02, incorporated by reference, discloses the AFP-31 and hAFP31 antibodies. [See in the Published application Fig. 1A, 1B, 5A and 5B for the complete nucleotide and amino acid sequences of the variable light and heavy chains of the antibodies; pages 40-55 for discussion of preparation of monoclonal antibodies, pages 55-57 for production of antibody fragments, pages 95-96 for expression vectors used, and Examples 5 and 6 for the PCR amplification, cloning and transfection protocols for preparing the humanized anti AFP-1 antibody.]

MN-14: U.S. Patent No. 5,874,540, filed 10/4/94 and issued 2/23/99 discloses the MN-14 antibody. [See Fig. 7 and 8 for complete nucleotide and amino acid sequences of the variable

heavy and light chains of the antibody; Examples 3-4 and 5-6 for the cDNA synthesis, PCR amplification, and cloning of the heavy and light chain variable regions, Example 8 for construction of suitable expression vector and expression of variable regions, and Examples 9 and 10 for expression and purification of the antibody.] Although this application was not incorporated by reference in the instant application, it was published and therefore, the antibody was publicly known at the effective filing date of the instant application.

These references demonstrate that the complete sequences, methods of production and use of all of these antibodies were known in the art prior to the effective filing date of the instant application of December 13, 2002. Applicant therefore submits that the claimed subject matter is fully enabled by the instant Specification, in light of general knowledge in the art, and that no deposit should be required for the antibodies stated in claims 63-66. Reconsideration and withdrawal of the rejections are respectfully requested.

New Claims 67-77 – CDR sequences of the antibodies LL1, hA20, RS7, PAM-4, Mu-9, AFP-31, hLL1, hRS7, hPAM4 and hMu9

All claimed CDR sequences were reported prior to the effective filing date of the instant application. CDR sequences claimed in Claim 67 (RS7 and hRS7) can be found in Figures 2A, 2B, 4A and 4B of application Ser. No. 60/360,229, filed 3/1/2002 which was incorporated in its entirety in the instant application at paragraph [0066]. CDR sequences claimed in claim 68 (LL1 and hLL1) can be found at Figures 1A, 1B, 4A and 4B of application 60/360,259 filed 3/1/2002. CDR sequences claimed in claim 69 (hA20) can be found in Figures 1A, 1B, 5A, 5B and 5C of the Application Ser. No. 60/416,232, filed 10/7/2002. CDR sequences claimed in Claim 70 (PAM-4 and hPAM4) can be found in Figures 1A, 1B, 4A and 4B of the application Ser. No. 60/388,314, filed 6/14/2002 which was incorporated in its entirety in the instant application at paragraph [0066]. CDR sequences claimed in Claim 71 (Mu-9 and hMu-9) can be found in Figures 1A, 1B, 4A and 4B of the application Ser. No. 10/116,116, filed 4/5/2002 which was incorporated in its entirety in the instant application at paragraph [0066]. CDR sequences claimed in Claim 72 (AFP31 and hAFP-31) can be found in Figures 1A, 1B, 5A and 5B of the application Ser. No. 60/399,707. CDR sequences claimed in Claim 73 (MN-14) can be found in Figures 7 and 8 of the U.S. Patent No. 5,874,540.

Although the applications disclosing hA20 and MN14 were not incorporated by reference in the instant application, these applications were published before the effective filing date of the instant application and thus, the CDRs of these antibodies were known at the time.

Therefore the Applicant respectfully submits that new claims 67-73 are allowable.

Claim Rejections - 35 USC §103

While Applicant traverses the obviousness type rejection, in the interests of advancing prosecution, Applicant has amended Claim 1 to include the limitations of Claim 10. Action had indicated that Claim 10, which depended from Claim 1, was free from prior art and would be allowable if written in independent form. Applicant has amended Claim 1 to include all the limitations of Claim 10. Amended Claim 1, therefore, is now allowable. Since Claims 13-15, 17, 19, 21-31, 33, 34, 36, 38, 40-44, 48-50, 63-77 depend from Claim 1 and contain all the limitations of claim 1 plus additional limitations, they are also allowable.

Similarly, Action had indicated that claims 18, 20, 32, 37, 39 and 45 would be allowable if written in independent form. Accordingly, Applicants have amended Claims 18, 32, 37 and 45 so that they are in independent form and no longer depend from a rejected independent claim. Since Claims 20 and 39 depend from amended Claims 18 and 39 and contain all limitations of these claims plus additional limitations and they are also allowable.

Conclusion

In conclusion, all of the claims remaining in this application should now be seen to be in condition for allowance. A prompt notice to that effect is respectfully solicited. If there are any remaining questions, the Examiner is requested to contact the undersigned at the number listed below.

Respectfully submitted,

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